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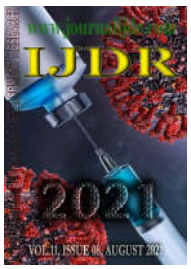

RESEARCH ARTICLE OPEN ACCESS

TUBERCULOSIS/HIV COINFECTION IN SÃO LUÍS, BRAZIL: ASSOCIATED FACTORS AND SPATIAL ANALYSIS

***[1]Darly Serra Cutrim, [2]Maria Nilza Lima Medeiros, [3]Silmery da Silva Brito Costa, [3]José de Jesus Dias Júnior, [4]Adriana Soraya Araujo, [5]Dalila de Nazaré Vasconcelos dos Santos, [3]Vanessa Moreira da Silva Soeiro, [3]Ana Patricia Barros Câmara, [3]Thaís Furtado Ferreira and [3]Maria dos Remédios Freitas Carvalho Branco**

[1]Programa de Pós-Gradução em Gestão de Programas e Serviços de Saúde. Universidade CEUMA; [2]Secretaria de Estado da Saúde do Maranhão; [3]Programa de Pós-Graduação em Saúde Coletiva. Universidade Federal do Maranhão; [4]Programa de Pós-Graduação em Saúde e Ambiente. Universidade Federal do Maranhão; [5]Escola Nacional de Saúde Pública Sergio Arouca/FIOCRUZ

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****Corresponding author: Darly Serra Cutrim,***

ABSTRACT

Objective: This study was to identify factors associated with Tuberculosis/HIV coinfection and conduct a spatial analysis of Tuberculosis/HIV cases in São Luís, the capital of the State of Maranhão. **Methods:** analytical cross-sectional study of confirmed cases of Tuberculosis/HIV coinfection. The analysis of the factors associated with Tuberculosis/HIV coinfection was performed using Poisson regression. The spatial analysis was performed using local and global Moran's indices and spatial lag regression. **Results:** Poisson regression showed a significant association between being male, alcoholism, and diabetes and Tuberculosis/HIV coinfection. The spatial model showed a positive correlation between population density and income and Tuberculosis/HIV coinfection. **Conclusion:** The factors associated with Tuberculosis/HIV coinfection were being male, alcoholism and diabetes.

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INTRODUCTION

Tuberculosis (TB) is the leading HIV-associated opportunistic disease and one of the main causes of death among people living with HIV (PLHIV) in developing countries (Antonucci et al., 1995). The increase in the global prevalence of TB/HIV coinfection poses a major challenge for the control of these diseases, particularly in those countries with high prevalence rates and limited health care resources (WHO, 2011). The lifetime risk of falling ill with TB among immunocompetent individuals infected with the TB bacillus is around 10%. In contrast, this risk is up to 10% per year among PLHIV not receiving antiretroviral treatment (Antonucci et al., 1995). The prevalence of TB/HIV coinfection in Brazil, in the State of Maranhão, and in São Luís in 2017 was 11.4%, 10.6%, and 12.7%, respectively (Ministério da Saúde, 2019). Various socioeconomic and demographic factors, such as low family income, malnutrition, inadequate housing, high housing density, migration, difficulties in accessing health services, and lack of access to social services, have been cited as risk factors for TB (Antonucci et al., 1995).

Various factors linked to TB have also been reported to be drivers of HIV risk behaviors, such as injection drug use, engaging in sex work, behavioral disorders, and lack of access to HIV testing and antiretroviral therapy (Peruhype et al., 2014). Spatial analysis is an important tool for identifying priority areas for public health interventions. The use of spatial analysis in studies investigating TB/HIV coinfection can help reveal spatial inequalities and associated factors and characterize risk areas (Vendramini et al., 2010).

Objective: The objective of this study was to identify factors associated with Tuberculosis/HIV coinfection and conduct the spatial analysis of Tuberculosis/HIV cases in São Luís, the capital of the State of Maranhão.

METHODS

We conducted an analytical cross-sectional study of all confirmed cases of TB/HIV coinfection in São Luís, Maranhão recorded from

January 2008 to December 2017 on the national notifiable diseases information system (SINAN - *Sistema de Informação de Agravos de Notificação*) using spatial analysis (SINAN, 2018). The following variables were extracted from the SINAN's TB investigation form: residential address (street name), area/neighborhood, zone (urban, peri-urban, rural), sex (male, female), race/color (white, black, yellow, brown, indigenous), year of notification, associated health problems (AIDS, alcoholism, diabetes, mental disorders, other). These data were initially entered into an Excel® spreadsheet and transferred to Stata® 14 after checking for and correcting inconsistencies and double entries. A descriptive analysis of the cases of TB/HIV coinfection was performed using the absolute and relative frequencies of each variable. To select the variables for the multivariate analysis we used logistic regression starting with a null model using the forward-stepwise method command in Stata® and adopting a significance level of p-value=0.20 for the variables included in the model and p-value=0.05 for the variables that stay in the model, followed by Poisson regression with robust variance estimation. The association between each variable and TB/HIV coinfection was tested using Poisson regression with robust variance estimation, comparing cases of TB/HIV coinfection with cases of TB without HIV coinfection. The TB/HIV coinfection incidence rate was calculated as the ratio between the number of cases of TB/HIV coinfection (numerator) and the total census tract population (denominator) multiplied by 100,000 inhabitants. The population data were taken from the 2010 census, conducted by the Brazilian Institute of Geography and Statistics (IBGE - *InstitutoBrasileiro de Geografia e Estatística*) (IBGE, 2010). Random variability was reduced by smoothing the incidence rates using empirical Bayes estimation. Naperian log transformation (Ln) was applied to the dependent variable (incidence of TB/HIV coinfection) to make the data set closer to a normal distribution. The spatial analysis was performed using the following socioenvironmental and demographic data obtained from the 2010 Census: population density; average number of household members, average household income; illiteracy rate; literacy rate; "subnormal" clusters (areas with poor living conditions); percentage of households not connected to the public water system; percentage of households without waste collection services; percentage of households with waste collection services; proportion of households with an accumulation of garbage in the surrounding environment;proportion of households exposed to open sewers in the surrounding environment; proportion of households not exposed to open sewers in the surrounding environment. The residence address of each case of TB/HIV coinfection was converted into a geographic coordinate using Google Maps, Bing Maps, and Wikimapia. The coordinates were then converted into points in a geodatabase using the ArcGIS 10.4.1 geocode function. Seventy (11.3%) of the 622 recorded cases were excluded because they did not have an address or had an incomplete address. The cases were then aggregated at census tract level using QGIS 3.6.0 and based on the map of São Luís obtained from IBGE's website and the 2010 census tract grid. The spatial autocorrelation and the spatial distribution of the smoothed TB/HIV coinfection incidence rate were measured using Global Moran's I and Local Moran's I (expressed on a LISA Map), respectively. A significance level of 5% was adopted for both indices. Global Moran's I was validated using the pseudo-significance test with 999 permutations. A spatial lag model was applied to incorporate spatial effects. This model is designed to capture the structure of spatial autocorrelation for a single parameter added to the standard regression model. We used GeoDa 1.14 to calculate the incidence rates, local empirical Bayes estimators, and local and global Moran's indices, and to apply the spatial model.

Ethical Aspects: This study was approved by the Research Ethics Committee of the University Centro Universitário do Maranhão (CEUMA) (code number 2.228.632).

RESULTS

Tuberculosis/HIV coinfection was found in 622 (11.68%) of the 5,326 cases of TB reported from 2008 to 2017. Patients with TB/HIV coinfection were predominantly male, black or brown, and had completed primary education. The results from the Poisson regression model showed an association between being male, alcoholism, and diabetes and TB/HIV coinfection (Table 1).

Table 1. Sociodemographic characteristics, bivariate modeling and multivariateof notified cases of tuberculosis/HIV coinfection. São Luís-MA, 2008-2017

Variables	Tuberculosis/HIV coinfection									
	No		Yes		Bivariate analysis			Multivariate analysis		
	N	%	N	%	PR*	CI** 95%	p-value	PR*	CI 95%	p-value
Sex	4703		622							
Male	3120	66.34	467	75.08	0.37	0.19-0.56	<0.001	0.72	0.59-0.87	<0.001
Female	1583	33.66	155	24,92						
Alcoholism	4612		611							
Yes	455	10.57	492	80.52	0.67	0.47-0.87	<0.001	1.75	1.44-2.11	<0.001
No	4156	89.41	119	19.48						
Notapplicable	1	0.02	0	0.00						
Diabetes	4621		611							
Yes	345	7.47	24	3.93	(-)0.61	(-)1.02 - (-)0.21	0003	0.86	0.37-0.84	0.006
No	4274	92.49	587	96.07						
Notdetermined	2	0.04	0	0.00						
Race	4652		612							
White	586	12.60	71	11.60						
Black	4062	87.32	541	88.40	(-)0.97	(-)0.34 - 0.14	0.433			
Yellow	2	0.04	0	0.00						
Indigenous	2	0.04	0	0.00						

*PR: Prevalence Reason **CI: Confidence interval. Source: SINAN (2018)

Table 2, Sociodemographic characteristicsandspatialmodelingof notified cases of tuberculosis/HIV coinfection. São Luís-MA, 2008-2017

Characteristics	Coefficient	Standard Error	T-test	p-value
Populationdensity	8.55999e-006	2.209e-006	3.87504	<0.001
Income	0.000199832	5.32283e-005	3.75424	<0.001
Rubbishcollected	-0.0084213	0.00286117	0.00325	<0.001
Not exposed to open sewers	-0.000177429	0.000177429	-2.85079	0.0043

The global Moran's I revealed a positive, statistically significant spatial autocorrelation for the smoothed TB/HIV coinfection incidence rate (I=0.21; p=0.001), while the local Moran's I (Figure 1) showed cores of clusters of census tracts with high smoothed TB/HIV coinfection incidence rates and neighbors with high rates in the Northwest, Central, East, and South regions.

The results of the final spatial lag model showed a positive correlation between population density (p<0.001) and average income (p<0.001) and the log-transformed TB/HIV coinfection incidence rate. In contrast, we found a negative correlation between percentage of households with waste collection services (p<0.001) and proportion of households not exposed to open sewers in the surrounding

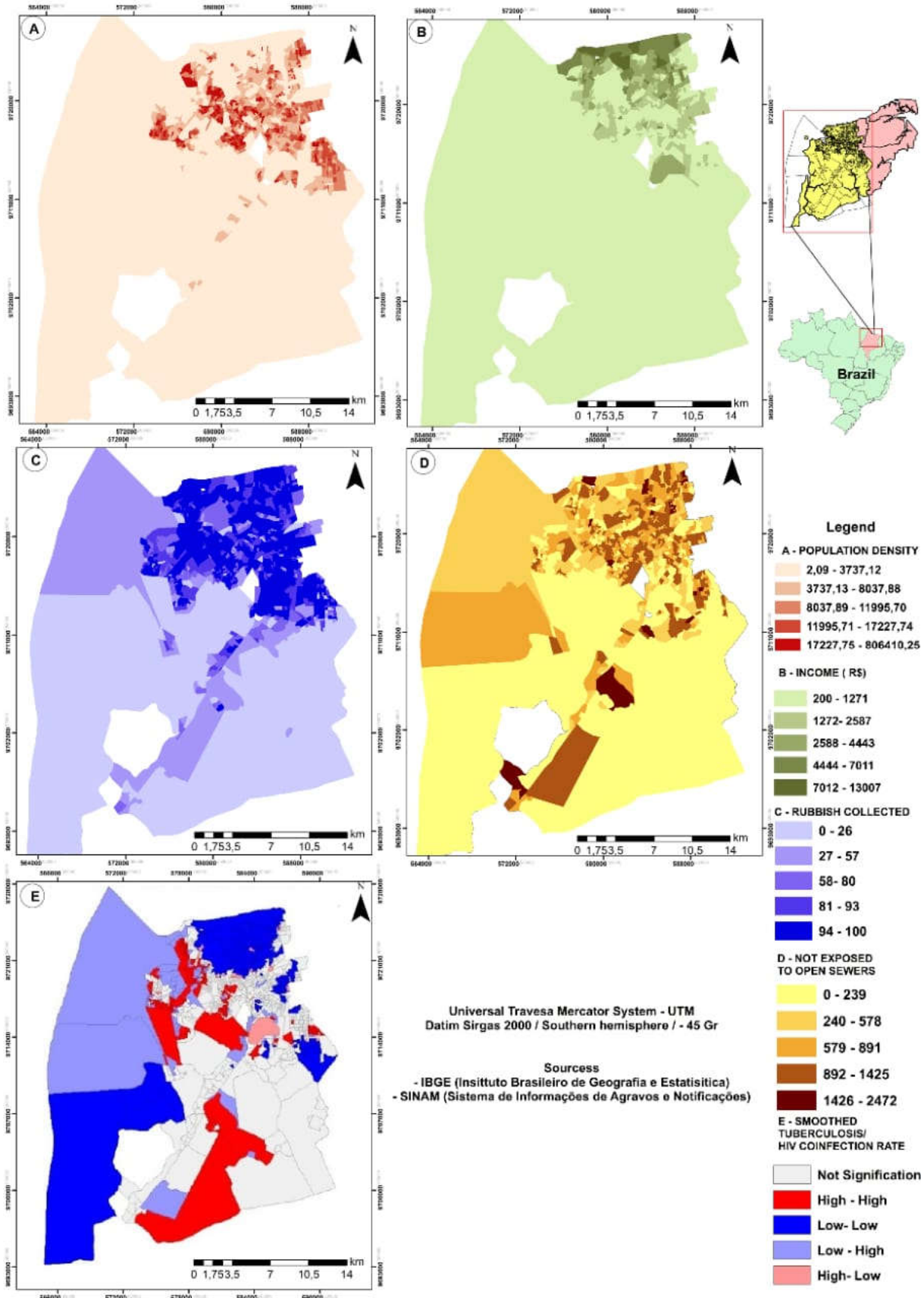

Figure 1. Spatialization of sociodemographic characteristics and Lisa Cluster Map showing Bayes smoothed tuberculosis/HIV coinfection incidence rates. São Luís-MA, 2008-2017

environment (p<0.0043) and the log-transformed TB/HIV coinfection incidence rate (Table 2). The R^2, log-likelihood, Akaike information criterion (AIC), and Schwarz criterion (SBC) for this model were 0.2178, -2606.49, 5224.98, and 5255.11, respectively.

DISCUSSION

Our findings show a significant association between being male, alcoholism, and diabetes and TB/HIV coinfection. The fact that TB/HIV coinfection is more frequent in men than in women may be explained by the fact that men are more vulnerable to both HIV and TB infection (Liberato et al., 2004). It is known that alcohol consumption, particularly excessive alcohol intake, can trigger risky sexual behavior, being associated with lower levels of condom use and/or having multiple sexual partners and thus leading to increased risk of HIV infection (Miller et al., 2016; Baluku et al., 2020). In the present study, having diabetes was associated with risk of HIV infection among individuals with TB. These results contrast with other studies reporting that individuals with TB without diabetes were more likely to be infected with HIV than those with diabetes (Prado et al., 2014; Moreira et al., 2019). However, there is strong evidence in the literature that uncontrolled diabetes is associated with various complications, for example increased susceptibility to infections, where hyperglycemia and reduced circulating insulin adversely affect immune response (Seiscentos, 2012; Ronacher et al., 2015). The spatial model showed that high population density and the presence of households without waste collection services and exposed to open sewers in the surrounding environment contributed to a high TB/HIV coinfection rate. In this respect, a study conducted in São José do Rio Preto in the State of São Paulo reported that the risk of TB/HIV coinfection is higher among people living in socially deprived areas (Vendramini et al., 2010). Conversely, studies in Porto Alegre (Peruhypeet al., 2014) and the State of MatoGrosso do Sul (Prado et al., 2020) also found high TB/HIV coinfection rates in better off areas, contrasting with national trends showing that TB predominantly affects socially excluded groups (Orfão et al., 2015).

Our findings also show a direct relationship between average household income and TB/HIV coinfection. However, TB/HIV coinfection does not affect only marginalized groups. Despite the strong link between low socioeconomic status and high rates of coinfection, evidence shows that coinfection is on the rise among people with higher socioeconomic status, demonstrating that there are two scenarios of TB occurrence: the traditional scenario, associated with poverty and socially excluded and marginalized groups; and coinfection with HIV, which cuts across different socioeconomic groups (Sousa et al., 2013). Historically, the control of TB at the primary healthcare level has faced several challenges, including lack of resources and inadequate staff training (Villa & Ruffino-Netto, 2009). On the other hand, Brazil's response to AIDS has been much more effective, receiving financial resources from both national and international governmental and nongovernmental organizations, probably contributing to the notification of cases of HIV and TB/HIV coinfection (Vendramini et al., 2006). The main limitation of this study is that it was not possible to georeference 70 (11.3%) of the cases of TB/HIV coinfection due the lack of an address/incomplete address. Strengths include: to the best of our knowledge, this is the first study in Brazil to identify an association between diabetes and TB/HIV coinfection; the spatial analysis of TB/HIV coinfection enabled the identification of priority areas for intervention; the use of a spatial regression model to investigate factors associated with coinfection; and the cases of TB/HIV coinfection were aggregated using the smallest geographic unit for which census data are available in Brazil, thus enabling a more detailed analysis.

CONCLUSION

The factors associated with TB/HIV co-infection in São Luís were male gender, alcoholism and diabetes and TB / HIV co-infection. Living with diabetes was associated with the risk of HIV infection among individuals with TB. In addition, the high population density, and the presence of households without garbage collection service and exposed to open sewage in the surroundings contributed to the high rate of TB/HIV co-infection, as shown in the spatial model. Our research also shows a direct relationship between the average family income and TB/HIV co-infection. Finally, several factors were related to the occurrence of TB/HIV co-infection, indicating the need for operationalizing public health policies that focus on both individual factors and social determinants of health.

Conflict of interest: The authors declare that there is no conflict of interest.

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